

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : MARTIN, et al.

U.S. Serial No.: Not Yet Known, corresponding to
International Application No.
PCT/US03/18716, filed June 13, 2003, which
claims priority of U.S. Serial No.
10/172,346, filed June 13, 2002

Filed : Herewith

For : IN-VIVO ENERGY DEPLETING STRATEGIES FOR
KILLING DRUG-RESISTANT CANCER CELLS

Law Offices of Albert Wai-Kit Chan, LLC
World Plaza, Suite 604
141-07 20th Avenue
Whitestone, NY 11357

December 10, 2004

Mail-Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, Applicants would like to direct the Examiner's attention to the following references which are listed below and on Forms PTO/SB/08A and PTO/SB/08B, which are attached hereto as **Exhibit A and Exhibits 1-9**.

1. Herceg Z. & Z.-Q. Wang. Failure of poly(ADP-ribose) polymerase cleavage by caspases leads to induction of necrosis and enhanced apoptosis. Mol. Cell Biol. 19:5124-5133 (1999)
2. Hirsch, T. et al. The apoptosis-necrosis paradox. Apoptogenic proteases activated after mitochondrial permeability transition determine the mode of cell death. Oncogene 15:1573-1581 (1997)

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8. Mehmet, H., et al. Relation of impaired energy metabolism to apoptosis and necrosis following transient cerebral hypoxia-ischaemia. *Cell Death Differ.* 5:321-329 (1998)
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16. PCT Written Opinion for Sloan-Kettering Institute for Cancer Research, et al., Int'l App'l No. PCT/US01/46886, Filed on December 4, 2001, Dated April 17, 2003
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18. PCT Notification of Transmittal of the International Search Report for Sloan-Kettering Institute for Cancer Research Application No. PCT/US03/18716, Filed on June 13, 2003, Dated November 25, 2003.

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51. Lu, et al., Cellular ATP Depletion by LY309887 as a Predictor of Growth Inhibition in Human Tumor Cell Lines. *Clinical Cancer Research*; January 1, 2000, 5:271-277. [Exhibit 3]
52. Venkatachalam, et al., Energy Thresholds That Determine Membrane Integrity and Injury in a Renal Epithelial Cell Line (LLC-PK1). *J. Clin. Invest.*; 1988, 81:745-758. [Exhibit 4]
53. Anundi, et al., Fructose prevents hypoxic cell death in liver. *The American Journal of Physiology*; 1987, Sep;253(3 Pt 1):G390-G396. [Exhibit 5]
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55. Yager, et al., Correlation between Content of High-Energy Phosphates and Phypoxic-Ischemic Damage in Immature and Mature Astrocytes. *Elsevier Science Publishers, Amsterdam*; 1994, 82(1-2):62-68. [Exhibit 7]
56. PCT International Search Report for Sloan-Kettering Institute for Cancer Research, et al., Int'l App'l No. PCT/US03/18716, Filed on June 13, 2003, Dated November 25, 2003. [Exhibit 8]

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57. WO 93/23014 A1 (Martin et al.) Chemotherapeutic Drug
Combinations, Published 25 November 1993 [Exhibit 9]

REMARKS

References 1-14 of the above-identified fifty-seven (57) references were submitted as Information Disclosure Statement to the United States Patent and Trademark Office on December 9, 2002 for U.S. Serial No. 10/172,346, filed June 13, 2002. References 15-16 of the above-identified fifty-seven (57) references were submitted as Supplemental Information Disclosure Statement to the United States Patent and Trademark Office on September 4, 2003 for U.S. Serial No. 10/172,346, filed June 13, 2002. Reference 17 of the above-identified fifty-seven (57) references was submitted as Supplemental Information Disclosure Statement to the United States Patent and Trademark Office on September 19, 2003 for U.S. Serial No. 10/172,346, filed June 13, 2002. Reference 18 of the above-identified fifty-seven (57) references was submitted as Supplemental Information Disclosure Statement to the United States Patent and Trademark Office on December 12, 2003 for U.S. Serial No. 10/172,346, filed June 13, 2002. Also, References 19-48 of the above-identified fifty-seven (57) references were submitted as Supplemental Information Disclosure Statement to the United States Patent and Trademark Office on May 19, 2004 for U.S. Serial No. 10/172,346, filed June 13, 2002. Accordingly, Applicants will not provide these documents unless otherwise requested by the Examiner. References 49-57 of the above-identified fifty-seven (57) references are attached herewith.

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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Respectfully submitted,

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First Named Inventor

Daniel S. MARTIN

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	1	Herceg Z. & Z.-Q. Wang. Failure of poly(ADP-ribose) polymerase cleavage by caspases leads to induction of necrosis and enhanced apoptosis. Mol. Cell Biol. 19:5124-5133 (1999)	
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		Application Number	Not Yet Known
		Filing Date	Herewith
		First Named Inventor	Daniel S. MARTIN
		Art Unit	Not Yet Known
		Examiner Name	Not Yet Known
		Attorney Docket Number	636-C-PCT-US
Sheet	5	of	7

OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	35	Martin, D.S., Stolfi, R.L., Sawyer, R.C., Spiegelman, S. Casper, E.S. and Young, C.W. Therapeutic utility of utilizing low doses of N-(phosphonacetyl)L-aspartic acid in combination with 5-fluorouracil; a murine study with clinical relevance. Cancer Res. 43:2317-2321, 1983.	
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Application Number

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First Named Inventor

Daniel S. MARTIN

Art Unit

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Examiner Name

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Attorney Docket Number

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	45	O'Dwyer, P.J., Judes, G.R., Colofiore, J., Walczak, J., Hoffman, J., LaCreta F.P., Comis, R.L., Martin, D.S., Ozols, R.F., Phase I trial of fluorouracil modulation by of N-phosphonacetyl-L-aspartate and 6-methylmercaptopurine riboside: optimization of 6-methylmercaptopurine riboside dose and schedule through biochemical analysis of sequential tumor biopsy specimens. J. Natl. Cancer Inst.; 1991, 83(17):1235-1240.	
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